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THE DEPENDENCE OF DIURESIS ON THE SALT CONTENT AND HYDROGEN ION CONCENTRATION OF DRINKING WATER

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This paper deals primarily with explaining tests which were carried out to determine the amount of urine excreted from different types of mineral waters and ordinary waters taken into the organism. Tests were made on a variety of German mineral waters, such as Ludwigsbrunnen, Muhlbrunn, etc. The tests were carried out on rabbits, dogs and the author also made tests on himself by drinking various types of water. Distilled water, sodium chloride solutions, tap water and various mineral waters were tested and the amount of excretion in ccm was measured during a four-hour period from one liter of the liquid which was imbibed.

It was found in these experiments that the amount of urine excretion depends upon the salt content of the liquid, the free carbon dioxide, the alcohol content, and the hydrogen ion concentration, among other factors. Salt content inhibits excretion; carbon dioxide stimulates it. The diuresis-stimulating effect of carbon dioxide is primarily due to the hydrogen ion concentration.

Author

Earlier investigations on the pharmacological effect of kidney function[1] /6 showed, among other things, that the Salck theorem[2] does not have any general validity, that "the water taken with food or in foods rich with water diluted the blood and was secreted in 6 to 7 hours". The amount of urine was found to be dependent upon: 1. the amount and distribution of the water which has been consumed according to the time of day or the meal times, 2. the composition, and 3. the manner of application of the consumed amount of liquid. As has been shown by the above-mentioned experiments, kidney function can, within certain limits, be completely independent of the amount of liquid consumed. Thus, in the case of a very limited supply of water, more of it is excreted than is

1. E. Starkenstein, Arch. f. exp. Path. u Pharmakol., 1962, Vol.92:339.
2. Falck, Zeitschrift fuer Biologie, 1872, Vol.8.

/Numbers in the margin indicate pagination in the original foreign text.

consumed, whereas in the case of a large supply of water which is evenly distributed, less of the water is excreted. This can only be traced back to the fact that in the case of a smaller supply, the water depots of the organism are acted upon, whereas, in the case of a larger supply they are filled up. The excretion of urine exceeds the supply only after the intake of very large amounts, the retention of which can no longer be handled by the tissue capacity. This case occurs when several liters of liquid are imbibed over an entire day or when approximately one liter is imbibed all at once.

In these experiments it was further found that, with the exception of /7 the factors mentioned, the amount of urine excretion is also dependent upon the salt content of the liquid supplied. The largest portion of a liter of tap water which is taken all at one time is excreted in the urine whereas the largest portion of a liter of Ringer solution or physiological sodium chloride solution supplied at the same time is retained. From this, the conclusion has been drawn that the isotonic liquid supplied to the organism can easily become stored water in the tissues, but this is not the case with the hypotonic liquid. It was concluded further that the amount of excreted water is in a constant ratio to the salt content of the water which is consumed. This fact also explains, as has already been emphasized in the first announcement on this subject[1], the findings of Else Aschenheim[2] and is completely consistent with the test results of Brunn[3] which were able to establish an inhibiting effect on secretion (in the case of the water experiments) after salt had been added, as well as with the test results of R. Meyer-Bisch[4] on the water econ-

1. Starkenstein, a. a. O.
2. E. Ascheinheim, Zeitschr. f. Kinderheilkunde 1919, Vol. 24.
3. F. Brunn, Zentralbl. f. innere Med. 1920, Vol. 41.
4. R. Meyer-Bisch, Zeitschr. f. d. ges. exp. Med. 1921, Vol. 24: 381 and Vol. 25: 295 and 309.

omy and in particular with his observation that injections of very small amounts of sodium chloride bring about retention of water in the tissues.

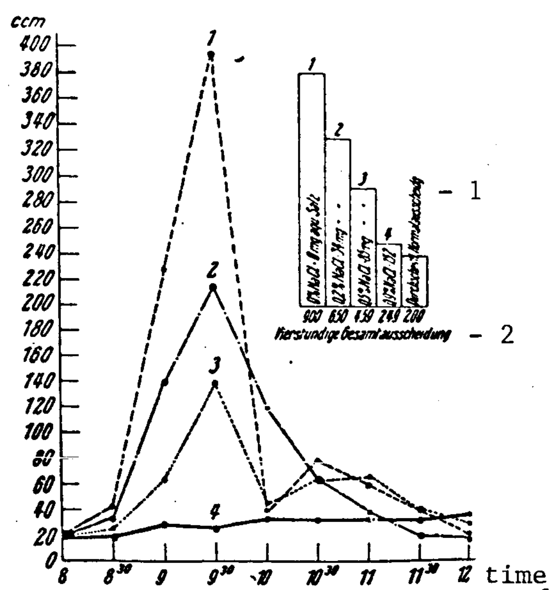
Table 1 and Curve 1 represent my tests on this matter.

TABLE I

Liquid Imbibed	Salt Content %	mg. Equivalent ‰	Ratio to Isotonicity 0.9% = 1	Amount in ccm Excreted from one Liter in 4 Hours	By Deducting the Average Normal Excretion of 200 ccm per 4 Hours there was Retained (ccm)
Distilled Water	0	0	0	900	300
Sodium Choloride Solution	0.2	34	0.22	650	550
Sodium Chloride Solution	0.5	85	0.55	459	741
Sodium Chloride Solution	0.9	153	1.0	249	951

Curve 1 gives the half-hour values for the excretion during the four hour test.

The dependence of the diuresis on the salt content of the imbibed water /8
must be standard for the diuretic effect of various mineral waters which, as is



1. Average Normal Excretion
2. Total Secretion for four hours

Curve 1

known, show in their total contents of mineral components (except for rare hypertonic waters) extreme differences of 2 - 150 mg. equivalents per kilogram.

In order to determine whether, in this connection, a regularity can be observed in the case of the individual mineral waters of different compositions, I have investigated, by means of tests on myself, always maintaining the same conditions, the excretion after intake of 1 liter of each of the mineral waters. During the morning, on an empty stomach, I drank one liter of the water being tested and then, every half hour over a period of 4 hours, I measured the excretion.

The results of these tests are given in Table 2, in which the figures in Table 1 have also been included.

Several tests were made with the various waters imbibed and there was thus obtained, by maintaining similar conditions, a good conformity. This also held true for similar tests on other persons.

When we compare Nos. 1, 4, 12 and 22 of the test series reproduced in /9
Table 2, we obtain, according to Table 1 for concentrations of 0, 5, 51 and 130 mg-Equivalent 0/oo, the descending excretion values of 90, 86, 61 and 38 ccm. These decreases in diuresis, corresponding to Table 1, with the salt content of the imbibed water are, however, only encountered in mineral waters exhibiting very great differences in concentration. On the other hand, if we compare the effects of mineral waters which differ to a lesser extent in this respect, we then obtain considerable deviations from this regularity.

Thus	Test	1	(distilled water)	mg-Equivalent %o	0	shows an excretion of	90%
but	"	3	(Richards source)	"	2	"	103%
	"	4	(Tap water)	"	5	"	86%
but	"	5	(Ludwigsbrunnen[1])	"	19	"	98%
	"	20	(Mühlbrunn)	"	87	"	67%
but	"	21	(Biliner)	"	91	"	80%
	"	22	(Karlsbrunnen)	"	130	"	38%
but	"	23	(Kreuzbrunnen)	"	142	"	49%

In the case of these portions in Table 2, the urine excretion after intake of water rich in salt is greater throughout than after intake of water which has a low salt content. Therefore, in these cases a second factor, in addition to the salt content, must have an effect on the amount of excretion.

A comparison of the qualitative composition of these waters in anions and cations did not provide any clue as to the explanation of this behavior. On the contrary, a clue appeared possibly with regard to the various contents of free carbon dioxide.

The composition of the waters used in the tests which is given in Table 2 makes it immediately recognizable that in the case of the test-pairs which have been compared against one another above (1:3, 4:5, 20:21, 22:23) a greater amount is excreted from that water which shows a greater degree of salt content and also a greater content of free carbon dioxide.

In order to verify the veracity of this assumption, there were carried out test-pairs 1:2, 6:6a, 11:11a, 21:21a and 26:27, and, finally, test 19.

Then, distilled water was saturated with CO_2 and in this way the excretion increased from 90% (1) to 123%. On the other hand, a saturation of Ringer solution with CO_2(27) only resulted in a dubious additional excretion of 3% in comparison with pure Ringer solution (24:27).

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By the same token, the excretion after intake of mineral water rich in CO_2 was compared with the excretion brought about by the same waters after being degassed. In test-pairs 11 and 11a the excretion of Waldquelle poor in CO_2 (old filling) was 53% less in comparison with the freshly filled water, rich in CO_2. The 21:21a test-pair provided similar results, in this case the effect of

1. Translator's note: Ludwigsbrunnen, Muhlbrunn, etc. refer to mineral waters from mineral springs named Ludwigsbrunnen, etc.

TABLE II

No.	Place of Source	Source	1 kg contains mg. equiv.	Ratio to isotonicity 153 to 171 mg. equivalent = 1	% excreted in 4 hours from 11 liter water drunk
1.	-	Distilled water	0	0	90
2.	-	Distilled water saturated with CO_2	0	0	123
3.	Konigswart	Richardsquelle	2	0.01	103
4.	Prag-Karany	Tap water	5	0.03	86
5.	Nauheim	Ludwigsbrunnen	19	0.12	98
6.	Giesshubel-Sauerbrunn	Fresh filling	26	0.17	90
6a.	Giesshubel-Sauerbrunn	Degassed	26	0.17	80
7.	Franzensbad	Nataliequelle	26	0.17	83
8.	Marienbad	Rudolphsquelle	30	0.19	84
9.	-	Sodium chloride solution 0.2%	34	0.22	65
10.	Krondorf	Stefaniequelle	34	0.22	83
11.	Marienbad	Forest source, fresh from the source	51	0.33	90
11a.	Marienbad	Forest source, old filling	51	0.33	52
12.	Ems	Kranchen	51	0.33	61
13.	Kissingen	Maxbrunnen	67	0.44	37
14.	-	Sodium chloride solution 0.5%	85	0.55	46
15.	-	Sodium chloride solution 0.5% + NaOH=n/100 NaOH-Sol.	85	0.55	48
16.	-	Sodium chloride solution 0.5% + HCl=n/40 HCl-Sol.	85	0.55	76
17.	-	Sodium chloride solution 0.5% + HCl=n/100 HCl-Sol.	85	0.55	65
18.	-	Sodium chloride solution 0.5% + acetic acid = n/40 acetic acid	85	0.55	57
19.	Konigswart	Richardsquelle	87	0.56	66
20.	Karlsbad	Muhlbrunn	87	0.56	67
21.	Bilin	Sauerbrunn	91	0.59	80
21a.	Bilin	Sauerbrunn, degassed	91	0.59	30
22.	Nauheim	Karlsbrunnen	130	0.84	38
23.	Marienbad	Kreuzbrunnen	142	0.92	49

TABLE II (Continued)

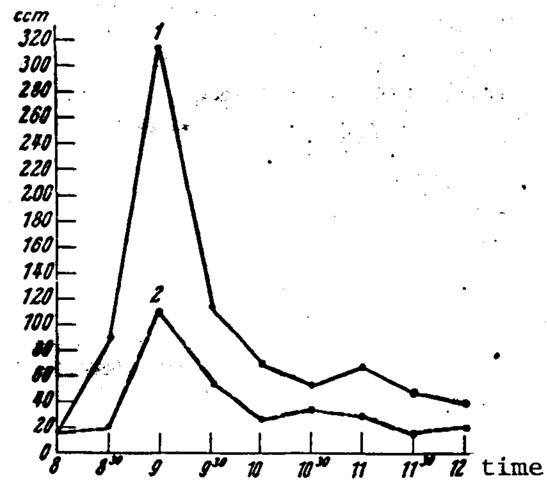
No.	Place of Source	Source	1 kg contains mg equiv.	Ratio to isotonicity 153 to 171 mg. equivalent = 1	% excreated in 4 hours from 11 liter water drunk
24.	-	Sodium chloride solution 0.9%	153	1.0	25
25.	-	Sodium chloride solution 0.9% + HCl=n/40 HCl-Sol.	153	1.0	31
26.	-	Ringer solution	171	1.0	24
27.	-	Ringer solution saturated with CO_2	171	1.0	27

TABLE II (Continued)

No.	1 kg of water consumed contains: Free sodium chloride, g	Millimol	Anions (mg-equiv.) Cl'	SO_4''	HCO_3'	Cations (mg-equiv.) Alkalies	Earths	Notations
1.	0	0	0	0	0	0	0	-
2.	?	?	0	0	0	0	0	-
3.	3.06	69.54	0.2	0.2	1.6	0.3	1.5	-
4.	0.017	0.42	0.31	0.51	3.2	0.31	4.2	-
5.	2.11	48.01	9.41	0.46	9.08	8.53	10.24	-
6.	2.72	61.72	0.41	0.37	25.06	18.22	7.54	pH 6.4
6a.	0	0	0.41	0.37	25.6	18.22	7.54	pH 7.4
7.	2.55	58.16	6	13.1	7.1	22	2.0	-
8.	2.0	50.0	1.3	2.0	27.1	7	22	-
9.	0	0	34.1	0	0	34.1	0	-
10.	2.76	62.9	0.37	0.22	33.5	17	15.8	-
11.	2.0	50.0	5.9	15.5	29.6	37	13	-
11a.	?	?	5.9	15.5	29.6	37	13	-
12	1.1	24.99	17.5	0.88	37	44.5	6.4	-
13.	2.05(?)	46.68(?)	46.80	6.10	13.11	45.62	21.31	Very old filling CO_2 content?
14.	0	0	85.4	0	0	85.4	0	-
15.	0	0	85.4	0	0	85.4	0	-
16.	0	0	85.4	0	0	85.4	0	-
17.	0	0	85.4	0	0	85.4	0	-
18.	0	0	85.4	0	0	85.4	0	-
19.	3.06	69.54	85.6	0.2	1.6	85.9	1.5	-
20.	0.68	15.46	17	35.3	34.5	76	10	-
21.	2.32	52.66	6.4	12.2	71.8	78	11	-
21a.	0	0	6.4	12.2	71.8	78	11	-
22.	1.84	42.01	121.1	1.01	7.96	110.93	19.09	-
23.	2.21	50.26	22.39	72.27	39.82	119.5	20.6	-
24.	0	0	153.9	0	0	153.9	0	-
25.	0	0	153.9	0	0	153.9	0	-
26.	0	0	168	0	3	167	4.0	-
27.	?	?	168	0	3	167	4.0	-

the Biliner Sauerbrunns free of CO_2 as compared with the effect of the natural water containing CO_2 was tested.

A decrease in excretion from 80% to 30% (thus 62% change) occurred as a result of the degassing. Curve 2 gives a graphical representation of the half-hour values during the four hours of testing. It also shows that the curves of the two tests follow exactly the same course in time[1].



Curve 2

Thus, it is evident from these curves that free sodium chloride actually increases the excretion of the imbibed water and that this effect is, however, influenced by the salt content of the water in question.

The CO_2 effect is not considerable in the case of hypotonic waters, be- /13 cause hypotonicity itself causes a high degree of excretion (compare Tests 6 and 6a). On the other hand, the effect of the CO_2 is insignificant in the case of isotonic waters. In this case, apparently the restraint in excretion caused

1. An absolute constant of curves of this type cannot always be expected; they vary slightly from day to day, but they essentially retain the same basic form. On the other hand, they change according to the composition of the water. Thus, in the above tests we see that the path of the curves is not altered by the removal of the CO_2, but simply that their highest points are lowered.

by the isotonicity can no longer be overcome by the CO_2. The effect of the carbon dioxide can be seen most clearly in the case of somewhat semi-isotonic waters as is distinctly shown by the 21:21a test-pair and especially well in test 19 and Table 3 which refers to the test. In this test, a "Richardsquelle" was used which, by adding sodium chloride, was brought to a salt content of 87 mg-Equivalent ‰, i.e., to approximately one-half isotonicity.

In this case the inhibiting effect of the additional salt was very clear, as was also the stimulating effect of the CO_2. While out of one liter 0.5% sodium chloride solution only 459 ccm was excreted and out of one liter of ordinary Richardsquelle 1030, 663 ccm was excreted starting with one liter of Richardsquelle 663 which was brought to one-half isotonicity. Therefore, here we see a decrease in the excretion of 36% due to the influence of the salt content. On the other hand, there was an increase in the excretion by 44% as a result of the CO_2 effect.

TABLE 3

Urine excretion in ccm after intake of one liter 8:00 in the morning on an empty stomach.

Time	Koenigswarter Richardsquelle	0.5% NaCL Solution	Richardsquelle brought to a 0.5% NaCL content
8:30	90	20	30
9:00	380	62	174
9:30	315	140	125
10:00	74	44	80
10:30	55	64	100
11:00	32	64	74
11:30	44	40	50
12:00	40	25	30
Total Excretion in 4 hours	1030	459	663

Carbon dioxide stimulates the diuretic effect of beverages, as has been known for a long time. Quincke[1] found that after taking beverages containing

[1]H. Quincke, Arch. f. exp. Path. u. Pharm. 1877, Vol. 77: 101

CO_2 the urine excretion is more abundant than after ordinary water is taken. /14
Quincke had already fully discussed the problem concerning the location of the point of contact of the diuresis-stimulating effect of the CO_2. He came upon four possibilities:

1. Passage of the CO_2 into the blood; from the blood into the kidneys where the CO_2 acts to promote excretion.

2. Central stimulation of the vasomotor nerves or the excretory nerves of the kidneys.

3. The CO_2 operates by stimulating the sensitive abdominal nerves reflectively to the nerves which participate in urine excretion, or

4. the CO_2 causes a more rapid resorption of the water which has been fed into the abdomen.

Possibilities 1 and 2 were rejected by Quincke because of the fact that, according to his calculations, even under the assumption of the most favorable conditions, the amounts of CO_2 remaining in the blood as a result of more rapid exhaling are much too small to produce any considerable effect, or an effect which is more than just transitional, on any of the organs. Possibility 3 then remained to be considered: reflective stimulation of the urine excretion by means of stimulation of the sensitive abdominal nerves. Quincke believes that in this case it is not a question of the amount of carbon dioxide water taken, but rather, that even an effervescent powder containing little water should lead to increased excretion. A test which he carried out in this regard provided him, however, with an opposite result, namely the urine excretion was reduced by the effervescent powder.

According to our tests above, this appeared quite understandable since the NaCl occurring in the abdomen from the sodium bicarbonate led to inhibition of the diuresis according to the experimental results described above. This experiment would not, therefore, justify the negative viewpoint of Quincke with respect to this third possibility.

For Quincke there remained only the third possibility: that the diuretic effect of the beverage containing carbon dioxide is caused by a more rapid resorption.

He also believes in the experimental fact that alcoholic beverages containing carbon dioxide, such as cider and sparkling wines, operate differently and have a more rapid intoxicating effect than ordinary wines; this can also be explained by their more rapid resorption.

It is evident from this presentation that Quincke has arrived completely by deduction at his assumption that the CO_2 stimulates the resorption starting from the abdomen, since experimental proof for the veracity of this assump- /15 tion, which has been taken as a proven fact in scientific literature, has not been made.

On the contrary, I was not able to observe in rabbits any stimulation of the resorption of water taken per os (through the mouth) as a result of the CO_2.

Also in the case of these animals, more was excreted from a liquid rich in CO_2 than from a liquid poor in CO_2. This was observed in several experiments on animals but, on the other hand, it is to be noted that this experiment did not always result in the same degree of accuracy as the experiment on human beings who had not eaten anything. In this case a great role is probably played in oral experiments by the consistently stuffed conditions of the stomach of the rabbit. Also in this case no effect of CO_2 was noted when using Ringer solution, but an effect was noted in the case of hypertonic solutions.

A direct experiment was made on an animal of this type to ascertain whether the CO_2 actually does accelerate the resorption in the stomach. Experiments of this type are easily carried out in stomachs which have been tied up. Thus, the stimulating effect of alcohol on the resorption is easily seen in a tied-up frog stomach: whereas an aqueous strychnine solution remains in the abdomen for 24 hours and does not lead to poisoning from here out, strychnine cramps occur in the same experimental pattern when an alcoholic strychnine solution is introduced into the abdomen. This experimental pattern was also used in this case for testing the resorption-accelerating effect of CO_2.

The pylorus was tied up in two hungry rabbits and then 100 ccm of ordinary Biliner aciduous spring water was introduced into the stomach of one of the rabbits and the same amount of degassed mineral water was introduced into the stomach of the other rabbit. The laparotomy wound was then sewn up and the animals then indicated a completely normal external behavior in the next few hours. The animals were killed six hours later and it was noted that in the case of both animals not even a small amount of the liquid was resorbed. Only about 3 ccm was absent. Thus, this experiment did not provide any criterion for the assumption of an accelerating effect of CO_2 on the resorption in the stomach. It does not appear necessary to assume such an effect on the intestine since the resorption takes place quickly enough by itself in this case.

It thus became probable that the CO_2, as such, has a diuresis-stimulating effect according to the resorption. This was to be decided most easily by /16 means of measuring the excretion after intravenous injection of mineral water containing CO_2 and mineral water which did not contain CO_2. Biliner Sauerbrunn was used. It was injected into the animals without and difficulty.

Experiments on various animals already showed that the differences

TABLE 4

Urine exretion after intravenous injection of natural mineral water free of CO_2 into a rabbit weighing 2840 grams. Feed: oats and tap water.

Date	Time		Urine	Remarks
January 8	Noon to 5 P.M. 5 P.M. to		15	Normal period
January 9	Noon		23	Normal period
		24 hours	38	Normal period
January 10		24 hours	35	Normal period
January 11		24 hours	35	Normal period
January 12		24 hours	39	Normal period
January 13		24 hours	38	Normal period
January 14	Noon Noon to 5 P.M. 5 P.M. to		- 35	60 ccm Biliner intravenously
January 15	Noon		110	
		24 hours	145	
January 16		24 hours	40	
	Noon Noon to 5 P.M.		- 7	60 ccm degassed Biliner intravenously
January 17	up to Noon		29	
		24 hours	36	
January 18		24 hours	34	
	Noon 5 P.M. to		- 25	60 ccm Biliner intravenously
January 19	Noon		140	
		24 hours	165	
January 20		24 hours	40	

observed after imbibing liquid also occurred in the case of parenteral intake. It proved, however, to be more suitable to undertake the experiment on the same animal. Such an experiment is given in Table 4.

The diuresis-stimulating effect of the carbon dioxide also appeared, therefore, after intravenous injection of aqueous solutions. The assumption /17 of an indirect effect of the CO_2 by means of accelerated resorption is therefore, at least, unnecessary, especially since the above experiment already contradicts any stimulating effect of carbon dioxide on the resorption of water.

As after oral intake in rabbits, the effect does not occur immediately after the injection, but rather, later than in the case of human beings where it begins much more quickly and also dies away more rapidly.

It was then to be determined whether the carbon dioxide, as regards its diuretic effect, acted renally or extrarenally. An increase in CO_2 in the urine after intake of beverages rich in CO_2 could at least have provided a clue for this situation even though it could not provide absolute proof. I have carried out such CO_2 determinations in the urine in the spontaneous experiments mentioned above without, however, finding any values which were beyond the physiological variations. For all that, this conclusion speaks more in support of an extrarenal point of application.

The determination as to whether this point of application is to be sought in the blood or in the tissues must be made by means of special experiments and, at this stage, only assumptions or instances can be gathered together which can perhaps provide an explanation. However, it is certainly decisive for the representation that an answer be given to the question of whether, in the case of the carbon dioxide effect, we are dealing with the effect of the anion or the hydrocarbonation. It is improbable from the very beginning that we are dealing here with a hydrocarbon effect since this physiological anion does not, at any rate, have any effect of this type in its salts and this effect, even if it did occur, would also not be covered up by the cation.

It is thereby probable that the diuretic effect is an H ion effect.

The measurements made by Michaelis prove that the H ion concentration in the mineral waters is influenced by the free CO_2.

L. Michaelis[1] determined the actual hydrogen ion concentration of several Karlsbad mineral waters by means of the gas-cell method and found at a test temperature of approximately 18° for Muhlbrunn: 1.2×10^{-4}, for Sprudel: 1.7×10^{-4}, for Marktbrunn: 2.9×10^{-4}.

After the mineral water was left standing in open, flat bowls, whereby /18 naturally the free carbon dioxide evaporated and the H ion concentration also became smaller, it still amounted at 19° to approximately 3.4×10^{-6} for Muhlbrunn; 3.5×10^{-5} for Sprudel; and 3.8×10^{-6} for Marktbrunn. For Giesshubler Ottoquelle we found, by means of the indicator method, pH = 6.4 and for degassed water pH = 7.4.

We thereby see that the hydrogen ion concentration of the mineral waters is generally relatively small. The hydrogen ion concentration proceeds from the dissociation of the free carbon dioxide and is considerably reduced through the dissociation effect by means of the hydrocarbonations which are present at the same time.

The conclusion that the diuretic effect of the carbon dioxide is a H ion effect leads us to the generalization that the diuretic effect of a solution depends upon its hydrogen ion concentration.

1. L. Michaelis, Zeitschr. f. Balneologie 1913/14, Vol. 6: 336; 1914/15, Vol. 7: 331. Zrchiv f. experiment Path. u. Pharmakol. Vol. 104.

A testing of this supposition by means of observing the urine excretion after intake of mineral water of varied hydrogen ion concentration showed, indeed, that a diuretic effect is due to the H ions. These experiments are clearly shown in Table 5.

The H ion concentration was not measured in these tests, but the necessary dilution was computed according to the dissociation constants of the minerals used, whereby the slight effect of the ions of the consumed salts remained disregarded.

It follows from Table 5, that a diuretic effect is due to the H ions (in /19
the case of intake) in the stomach. This effect increases with an increase in concentration.

In these tests I drank, on the individual test days, four different solutions, i.e., in each case one liter with a pH content of approximately 1.5, 2.0, 3.0 and 7.0.

As is shown by the tests, from one liter of the above sodium chloride solution with 85 mg. equivalents and pH 7.0, 459 ccm were excreted in four hours. This excretion amounted in pH 1.5 to an increase by 65%, in the case of pH 2.0 to an increase by 40% and in the case of pH 3.0 to an increase by 19%. The progress of this set of experiments clearly indicates a dependence of the imbibed water on its content of hydrogen ions.

As in the case of carbon dioxide, the diuresis-stimulating effect of the H ions is also limited here by the salt content of the solution, inasmuch as in the case of isotonic solutions the inhibiting effect of the salts predominates over the stimulating effect of the H ions, so that with a 0.9% sodium chloride solution and pH 1.5 the increase in diuresis amounts to only 39% as compared with 65% with the 0.5% sodium chloride solution of the same pH.

TABLE 5

/18

Time	0.5% NaCl solution + HCl = $\frac{n}{40}$ HCl = pH 1.5	0.5% NaCl solution + HCl = $\frac{n}{100}$ HCl = pH 2	0.5% NaCl solution + acetic acid = $\frac{n}{40}$ = pH 3
	After intake of 1 liter liquid at 8 A.M. results in excretion		
8:30	65	30	40
9:00	200	90	170
9:30	140	232	102
10:00	80	44	95
10:30	95	70	47
11:00	90	70	60
11:30	50	60	35
12:00	40	50	25
Total excretion in 4 hours	760	646	574

TABLE 5 (Continued)

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Time	0.5% NaCl solution = pH 5	0.5% NaCl solution + NaOH = $\frac{n}{100}$ NaOH = pH 12	0.9% NaCl solution + HCL = $\frac{n}{40}$ HCL	0.9% NaCl solution
	After intake of 1 liter liquid at 8 A.M. results in excretion			
8:30	20	20	20	30
9:00	62	40	30	40
9:30	140	154	27	60
10:00	44	58	36	37
10:30	64	50	34	45
11:00	64	80	34	40
11:30	40	60	32	30
12:00	25	20	36	30
Total excretion in 4 hours	459	482	249	312

The possibility was further thought of that in alcoholic solutions, i.e., those with pH > 7.07, an additional inhibition in the diuresis could occur. In order to obtain an explanation to this, I then drank one liter of 0.5% sodium /20 chloride solution with a NaOH content of n/100 NaOH under the same test conditions, corresponding to pH=12. As the above experiments showed, however, the excretion in this case drops entirely in the range of excretion of neutral solutions of pH7, so that it can appear probable that a sudden change towards the alkaline side, at least with the order of magnitude given here, does not result in any noteworthy change in excretion.

Thus we have not given any specific effect of the sodium chloride in the diuresis-stimulating effect of sodium chloride in the mineral water, but rather a general characteristic of the acids or of the hydrogen ion concentrations.

At any rate, this effect of hydrochloric acid solutions and acetic acid solutions is a bit weaker than that of isohydrous CO_2 solutions.

The waters which are weakest in hydrocarbonate and richest in free Co_2 should fluctuate in an order of magnitude of pH 4.0. Test 19 in Table 2, however, shows us that in this H ion concentration which amounts to about pH 4.0, the diuresis is still stronger than in the case of the H ion concentration brought about with pH 3.0.

On the basis of these tests it can be assumed that still other factors play a role in modifying or increasing the effect of carbon dioxide on the diuresis.

It has also been shown (see Winterstein) that the CO_2 effect is in many cases an H ion effect. Even the narcotic effect of CO_2 can be placed side by side with the narcotic stage of resorptive acid poisoning (Walter-Schmiedeberg) and with diabetic coma.

In attempting to interpret the CO_2 effect as an H ion effect, it should not be overlooked that all acids having a greater dissociation constant than that of CO_2 must liberate the CO_2 from the hydrocarbonation which is present everywhere in the organism and that, conversely, all H ion effects can also be interpreted as CO_2 effects, i.e., as a molecular effect and not as an ion effect.

If we take the view, or if it is proven by further research in this area that we are actually dealing with an H ion effect, then the problem as to the more specific extrarenal type of application of the diuretic effect of the CO_2 becomes considerably simpler and then the determining factor possibly becomes the ratios of the H ions to the colloids.

If the H ion does actually play the role of a diuretic, then its changing concentration is significant to both the normal physiological diuresis and the pathological diuresis. In this respect we should bear in mind the change occurring in the H ion content of the organism during stomach digestion, in which case ample amounts of H ions are taken away from the organism and then, during a subsequent phase of digestion, once more flood the organism during resorption in the small intestine. /21

A test carried out on the hourly values of the 24-hour diuresis also indicated a wide dependence upon the meals, in the sense that in practically all cases there is a reduction in diuresis after the main meals and particularly as regards the amount of water taken during the meals. More precise tests in this regard will show to what extent the inhibition in the water excretion is due to the salts which are taken at the same time, or to the displacement of the liquid and ions in the organism during digestion.

Acidosis can perhaps also be considered as a contributing factor in diabetic polyuria, but in this case the conditions are surely not very simple when we consider that the subacidotic rabbits fed with oats usually excrete very little urine of high acid content in comparison with rabbits fed alkaline fodder who excrete a great deal of alkaline urine. Here, also, there should be taken into consideration the unequally larger water intake of the animals fed with fodder.

On the whole, it appears in problems concerning diuresis, that the results obtained in tests on human beings, dogs and rabbits have absolute validity generally only for the species in question and do not at all provide (as long as this has not been experimentally established) any generalization for the problem of diuresis.

SUMMARY

1. Earlier tests showed that the smaller the salt content in the water, the more of it is excreted in the urine over a four-hour period. Thus, the greatest portion of one liter of distilled water is eliminated through the kidneys in four hours, but, on the other hand, the greatest amount of one liter of physiological sodium chloride solution is retained in the body. This retention capacity increases parallel with the salt content up to isotonicity of the blood.

2. The diuretic effect of mineral waters is not only a result of their salt content, but is a complicated result of their salt and carbon dioxide content. The salt content inhibits the excretion of the imbibed water; the car- /22
bon dioxide content promotes the excretion of the imbibed water.

3. Under the given test conditions, in no case was excessive diuresis observed with the mineral waters. In this case it was exclusively a question of the amount of excretion of the imbibed water, i.e., its deposition in the organism.

4. The diuresis-stimulating effect of carbon dioxide is not unrestricted,

but it is limited by the salt content of the water concerned. This effect is most evident in semi-isotonic waters.

5. The diuresis-stimulating effect of carbon dioxide is not, as had been previously assumed, to be traced back to a resorption-stimulating effect of the carbon dioxide from the stomach out, but it is primarily caused by the hydrogen ion concentration which very generally has a diuresis-stimulating effect.

6. The factors which determine the amount of excretion of imbibed water during the four-hour test are therefore: (a) the hydrogen ion content (caused in mineral waters on the one hand by free CO_2 and on the other hand by hydrocarbonation), (b) the equivalent concentration of salts and the isotonicity ratio thus brought about.

7. Generally speaking, a CO_2 solution has a less stronger diuretic effect than an isohydrous solution of other acids.

8. The diuresis-inhibiting effect of the salts is to be traced back to extrarenal causes, just as is the diuresis-stimulating effect of CO_2 or H ions.

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